ABSTRACT OF THE DISCLOSURE

The eukaryotic mRNA 5' cap structure is recognized by eIF4E, which plays an essential role in translational control and cell growth. Members of a family of proteins called eIF4E-binding proteins (4E-BPs) inhibit the activity of eIF4E and consequently repress translation. Following exposure of cells to hormones, cytokines and growth factors, 4E-BPs become hyperphosphorylated and dissociate from eIF4E, to relieve translation inhibition. The phosphorylation events leading to 4E-BP1 dissociation from eIF4E are mediated by the PI3-kinase/FRAP/mTOR signaling pathway. The present study addresses the biological importance of 4E-BP1 *in vivo* by disrupting its gene in the mouse. Homozygous 4E-BP1 deficient mice are healthy and develop normally. However, they show an important decrease in white adipose tissue and blood glucose level, and the males show a decrease in total body weight and an increase in resting metabolic rate. Primary mouse embryo fibroblasts show accelerated cell growth and enhanced cap-dependent translation, coincident with an increase in eIF4E phosphorylation.